Brain Stem Hemorrhage in a 2-Year-10-Month-Old Child with Renovascular Hypertension Related to Fibromuscular Dysplasia

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Renovascular hypertension due to fibromuscular dysplasia is an uncommon but important cause of pediatric hypertension. It is usually ignored and diagnosed after a long delay because blood pressure is infrequently measured in children. We report a case of previously undiagnosed renovascular hypertension complicated with right renal infarction in a 2-year-10-month-old child, who initially presented as a case of conscious disturbance. The patient’s brain CT displayed brain stem hemorrhage, and a brain MRI showed acute hemorrhage and multiple old intracerebral hemorrhage. Therefore, intimal fibromuscular dysplasia of the right renal artery was diagnosed by computed tomography and confirmed after renal angiography. Her blood pressure was gradually normalized after medical therapy, including use of Losartan. She is presently asymptomatic on OPD follow-up. The importance of BP measurement can not be overemphasized in pediatric patients less than three years of age with underlying diseases.

Key Words: Conscious disturbance • Fibromuscular dysplasia • Renovascular hypertension

INTRODUCTION

Hypertension in children and adolescents is defined as, after repeated measurement, systolic blood pressure (BP) and/or diastolic BP ≥ 95th percentile.1 Renovascular hypertension is an important cause of hypertension in children.1,2 It is usually ignored and diagnosed after an extended delay because BP is infrequently measured in children.2 High BP values are generally dismissed as inaccurate, and BP percentile are commonly underestimated.3 The main causes of pediatric renovascular hypertension include Takayasu disease and fibromuscular dysplasia. Takayasu’s arteritis is common in Eastern countries, while fibromuscular dysplasia (FMD) is common in Western countries.4 Here we report a 2-year-10-month-old girl with previously undiagnosed FMD-related renovascular hypertension and right renal infarction initially presenting as conscious disturbance.

CASE REPORT

A 2-year-10-month-old girl was brought to our pediatric emergency department due to a change of consciousness. She had a past history of proteinuria and several episodes of facial palsy without any documented BP record. There was no history of Kawasaki disease, Williams syndrome, fever, head injury, drug ingestion, other vasculitis or recent illness. There was also no family history of neurofibromatosis, hypertension or stroke. The child complained of headache and vomiting...
before being sent to our hospital.

Upon initial evaluation, the patient was found to have hypertension (133/64 mmHg) and drowsy consciousness (Glasgow coma scale E3V3M5). Neurological examination revealed right and left pupil sizes 2.5/2.5 mm with light reflex, left facial palsy, Cheyne-Stokes respiration, normal muscle power and deep tendon reflex, absence of meningeal signs, and positive Babinski sign. Initial laboratory study showed normal sodium level (142 mEq/L), severe hypokalemia (2.4 mEq/L), high troponin-I level (1.249 ng/ml), proteinuria (> 300 mg/dl), and hematuria (> 100/HPF). Emergency computed tomography (CT) of the patient’s brain displayed brain stem hemorrhage (Figure 1A), and intravenous mannitol and potassium chloride were administered immediately. Under the preliminary diagnosis of intracranial hemorrhage and hypertension, she was admitted to the pediatric intensive care unit.

The patient received further antihypertensive treatment with labetalol and regained consciousness gradually on admission day 3. However, transient hypertension up to 198/167 mmHg was still noted. Fundoscopic examination revealed no papilledema or hypertensive retinopathy. Echocardiography showed left ventricle hypertrophy and diastolic dysfunction. MRI of the brain revealed acute hemorrhage (Figure 1B) and multiple old intracerebral hemorrhages. Additionally, further investigation for secondary hypertension was done. Serum thyroid hormones, catecholamines, cortisol and 24-hour urinary vanilmandelic acid and metanephrines levels were all within normal limit. Plasma renin activity (PRA) was 287.4 pg/mL. Aldosterone level was more than 1,000 pg/mL. The patient’s abdomen sonogram showed no adrenal tumor, but did reveal a small right kidney (sizes of right/left kidney 6.18/7.41 cm, respectively). Computed tomography of the abdomen showed wedge-shaped hypodensities of the right kidney with upper and lower pole infarcts. Computed tomography angiography (CTA) (Figure 2A) showed diffuse right renal artery stenosis with distal aneurysm. Magnetic resonance angiography (MRA) also revealed small right renal artery with distal aneurysm (Figure 2B). Tc-99m diethylene trimine pentaacetic acid (DTPA) renal scan without and with captopril showed left/right glomerular filtration rate (GFR) of 58.8/31.1 and 48.0/25.0 ml/min, respectively. Therefore, renal artery stenosis due to intimal fibromuscular dysplasia was diagnosed. Renal artery angiography confirmed the diagnosis of diffuse small right renal artery with distal aneurysms (Figure 2C), and angioplasty was not performed because of the lack of pressure gradient or focal stenosis. PRA levels of the right and left renal vein were > 340 and 185.6 pg/ml, respectively. In addition, MRA of the artery above the diaphragm for survey revealed negative findings. Vasculitis or thromboembolic disease were excluded after a series of workups, including those for C reactive protein (CRP), antinuclear antibodies (ANA), and protein-C, etc. The final diagnosis of FMD related to right renal artery stenosis and infarction with secondary hypertension and intracranial hemorrhage was made. Because DTPA renal scan with captopril showed decreased GFR in this patient, angiotensin-converting-enzyme (ACE) inhibitor and angiotensin receptor blocker were not chosen as first-line antihypertensive agents. Hypertension was treated with combination drugs (labetalol, amlopidine, hydrochlorothiazide), but fluctuated. After adding losartan, her BP was well controlled, and the patient was discharged in stable condition. She has been followed up for about 1.5 years after discharge. Her BP is around 100/60 mmHg under multiple antihypertensive drugs (labetalol, amlopidine, hydrochlorothiazide, and losartan) during follow-up. To the present, the patient suffers no neurological deficit.

**DISCUSSION**

The prevalence of pediatric hypertension in the larger population is 1-2%. One important common
cause of pediatric hypertension is renovascular diseases, which is secondary to coarctation of the thoracic aorta and parenchymal renal disease. The main causes of pediatric renovascular hypertension include Takayasu disease and fibromuscular dysplasia. Takayasu arteritis is common in Eastern countries, while FMD is common in Western countries. The gold standard for diagnosis of renal artery stenosis is catheter-based angiography. In the present case, the patient’s angiographic imaging indicated that renal artery stenosis was intimal FMD after exclusion of other diseases. Vasculitis (such as Takayasu disease) or thromboembolic disease were excluded after a series of workups, including normal CRP, negative ANA, and normal protein C. A few pediatric diseases, including Kawasaki disease, neurofibromatosis, and Williams syndrome were also excluded by the taking of patient histories and physical examination. To the best of our knowledge, this is the first pediatric case report about intimal FMD complicated with renal infarction and intracranial hemorrhage in Taiwan.

The initial diagnostic hint of this case was hypertension and hypokalemia. The high serum aldosterone and renin level further pointed to a possible diagnosis of renovascular hypertension. Diffuse right renal artery stenosis with distal aneurysm was shown by CTA/MRA, and confirmed by renal angiography. There were no other vascular lesions or evidence of vasculitis. Our finding is compatible with the diagnosis of FMD, which is a noninflammatory, and nonatherosclerotic arterial disease most commonly with involvement of the renal and carotid arteries. It occurs most frequently in women between 20 and 60 years of age, but may be encountered in the pediatric population. The initial manifestations of FMD in young children may be stroke and are quite different from those found in adults. According to pathological diagnosis, FMD is classified into intimal, medial, and adventitial types. This classification needs revision by angiographic appearance because most patients are now managed with percutaneous angioplasty. In the present case, there was diffuse dysplasia of the right renal artery without typical string of beads appearance, so the diagnosis of intimal FMD was favored. Intimal FMD accounts for about 10% of all types of FMD and occurs frequently in the pediatric population. In a minority of patients, the disease progression can de-
velop aneurysm, dissection, or infrequently occlusion which may explain the angiographic appearance and renal infarction of our patient.7

The primary goal in treating our patient is control of BP to prevent further sequelae of long-standing hypertension. Percutaneous transluminal renal angioplasty is a priority to help cure the patient.4 Zhu et al. demonstrated percutaneous transluminal renal angioplasty with a success rate of 94.1% is an appropriate treatment for FMD.4 However, percutaneous transluminal renal angioplasty was not performed because of the diffuse small diameter of the right renal artery without focal stenosis in our patient. Surgical revascularization is an alternative treatment to percutaneous angioplasty.8 In the present case, vascular surgery for distal renal aneurysm and stenosis was unfeasible because of technical difficulty. Nephrectomy was only indicated when a small, poorly functioning kidney was driving the hypertension.7 This patient’s hypertension was well controlled after adding losartan into the combination therapy. Losartan was reported to dilate the renal artery by suppressing intimal hyperplasia.9 Reversible FMD was also been reported to occur in a patient after an appropriate antihypertensive treatment without angioplasty.10 According to these previous reports, there is no indication for nephrectomy, and the best choice is to adopt a “wait and see” attitude for this patient under optimal medical therapy.

CONCLUSIONS

To conclude, a clinical presentation of FMD in young children is quite different from adults. Stroke may be an initial manifestation of FMD with a diagnostic challenge in pediatric patients. Although percutaneous angioplasty is the treatment of choice, it may be unsuccessful technically or not suitable when small vessel diameter is involved. Associated hypertension may be difficult to treat and could require multiple antihypertensive drugs such as calcium-channel blocker, β blocker, diuretic and an angiotensin-receptor blocker. Target organ damage, such as renal function impairment and stroke, should be followed up. The importance of regular measurement of BP in pediatric patients less than three years of age with underlying diseases cannot be overemphasized, to best prevent delayed diagnosis and treatment.

CONFLICT OF INTEREST STATEMENT

None declared.

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